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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,544	10/17/2001	Ira G. Schulman	509132000100	7779

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/982,544	SCHULMAN ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,16,17,21-23,30,31,34 and 36* is/are pending in the application.

4a) Of the above claim(s) *1-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,16,17,21-23,30,31,34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 1-13, 16, 17, 21-23, 30, 31, 34 and 36 are pending.

Applicants' amendment filed October 16, 2003 is acknowledged. Applicants' response has been fully considered. Claims 13, 17, 21, 22, 30, 31, 34 and 36 have been amended, and claims 15, 19, 20, 24, 26-29, 32, 33 and 35 have been cancelled. Claims 1-12 are non-elected inventions, thus are withdrawn from consideration. Therefore, claims 13, 16, 17, 21-23, 30, 31, 34 and 36 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claims 29, 32 and 33, under 35 U.S.C.112, first paragraph, is withdrawn in view of applicants' cancellation of the claim in the amendment filed October 16, 2003.

3. The previous rejection of claims 13, 16, 17 and 21-23, under 35 U.S.C.112, second paragraph, is withdrawn in view of applicants' amendment to the claim, and applicants' response at pages 12-13 in the amendment filed October 16, 2003.

Claim Rejections - 35 USC § 102

4. The previous rejection of claim 13 under 35 U.S.C. 102(a) as being anticipated by Shan *et al.* (WO 01/03705) is withdrawn in view of applicant's amendment to the claim, and applicants' response at page 13 in the amendment filed October 16, 2003.

Claim Rejections - 35 USC § 103

5. The previous rejection of claims 13 and 16 under 35 U.S.C. 102(3) as being as being unpatentable over Shan *et al.* (WO 01/03705) taken with Piper (US 2002/0177602 A1) is withdrawn in view of applicant's amendment to the claim, and applicants' response at page 13 in the amendment filed October 16, 2003.

Claim Objections

6. Claims 16 and 23 are objected to because the claim contains recitation of non-elected "additional active agents".

In response, applicant indicates claims 16 and 23 are dependent claims that define a Markush group of additional active agents to be used in combination with an LXR agonist in the claimed method, these agents are secondary agents in the method and are known in these types of therapies, thus this Markush class does not present a search burden, and the election of "thiazolidinedione" is a species election within a Markush group. The response has been fully considered, however, the argument is not found persuasive because each active agent cited in the claim is structurally different, and has different function and utility, while compounds included within a Markush group must share a common utility and share a substantial feature disclosed as being essential to that utility (See MPEP 803.02). Thus, each active agent is considered patentably distinct and this is not species election. Furthermore, the inclusion of additional

active agents would also yield search burden for the Examiner because these structurally and functionally agents must be search separately. Therefore, only the elected thiazolidinedione as the additional active agent is examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 13, 16, 17, 21-23, 30, 31, 34 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating diabetes type II comprising administering a specific LXR agonist, compound 1 (structure shown at page 30, paragraph 0105), does not reasonably provide enablement for a method for treating, or reducing the risk of developing or recurrence of diabetes, or treating type II diabetes comprising administering an LXR agonist, wherein the structure of the LXR agonist is not defined. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 13, 16, 17, 21-23, 30, 31, 34 and 36 encompass a method for treating or reducing the risk of developing or recurrence of diabetes comprising administering an LXR agonist (claims 13, 16, 17 and 30-31), or a method for treating type II diabetes comprising administering an LXR agonist (claims 21-23, 34 and 36). The specification, however, only discloses cursory conclusions (pages 3-4) without data supporting the findings, which state that the present invention provides methods for preventing, halting or slowing the progression of metabolic

diseases such as atherosclerotic cardiovascular diseases and related conditions in mammals by administering an LXRβ selective agonist, or for treating type II diabetes by administering an LXR agonist, or treating the complication of obesity such as type II diabetes by administering an LXRα selective antagonist. There are no indicia that the present application enables the full scope in view of treating or reducing the risk of developing or recurrence of diabetes or treating type II diabetes by administering an LXR agonist. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the treating conditions for reducing the risk of developing, or the risk of recurrence of diabetes, and the use of various LXR agonists, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for the use of a specific pan-LXR agonist, compound 1 in the treatment of type II diabetes in the mice model (pages 38-39, paragraphs 0121-0122, Fig. 15).

(3). The state of the prior art and relative skill of those in the art:

The related art (e.g., Shan *et al.*, WO 01/03705) indicates an LXR agonist having general formula ($C(R^1)(CX^1X^2X^3)(CX^4X^5X^6)(Ar\text{-}Y\text{-}R^2)$) can be used to treat atherosclerotic cardiovascular diseases and related conditions. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on how to monitor reducing the risk of developing or the risk of recurrence of diabetes, and the effects of various LXR agonists in the treatment to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for treating or reducing the risk of developing or the risk of recurrence of diabetes, or treating type II diabetes comprising administering an LXR agonist. The specification indicates the treatment of wild type mice with a specific pan-LXR agonist, compound 1 results in significant increase in high density lipoprotein (HDL, paragraph 0109, Fig 5) and compound 1 can reduce hyperglycemia (elevated blood glucose) in the diabetic mice (pages 38-39, paragraphs 0121-0122, Fig. 15). However, the specification fails to identify any other LXR agonists than compound 1, nor indicates the effect of various LXR agonists in the treatment of diabetes or type II diabetes. Moreover, the specification has not shown the treating conditions for reducing the risk of developing or the risk of recurrence of diabetes using an LXR agonist. There are no working examples indicating the claimed methods using various LXR agonists which have different structures. Furthermore, the specification does not provide any specific guidance as to how to monitor reducing the risk of developing or the

risk of recurrence of diabetes, for example, the dosage, the time of the treatment and how the effect of the compound on diabetes being monitored if the disease is still developing. Since the specification fails to provide sufficient teachings on the use of various LXR agonists, and how to monitor reducing the risk of developing or the risk of recurrence of diabetes diabetes, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of various LXR agonists.

(5). Predictability or unpredictability of the art:

The claims encompass treating, or reducing the risk of developing or the risk of recurrence of diabetes using an LXR agonist, however, the identities of various LXR agonists and the effects of various LXR agonists in treating or monitoring reducing the risk of developing or the risk of recurrence of diabetes are not described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(6). Nature of the Invention

The scope of the claims includes treating or reducing the risk of developing or the risk of recurrence of diabetes or treating type II diabetes using an LXR agonist, but the specification does not show the identities and the use of various LXR agonists in the treatment or reducing the risk of developing or the risk of recurrence of diabetes. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed methods, and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the outcome of the treatment using various LXR agonists. Thus, practice of the full scope of the

presently claimed invention based upon the current claims requires the practice of undue experimentation.

In response, applicants indicate the specification provides data supporting the findings regarding the claimed method, e.g., pages 30-39 and Figs. 1-15, especially paragraph [0121] and Fig. 15 for compound 1; and numerous LXR agonists are known in the literature and available for use in the claimed method without undue experiments, e.g., six publications or patents that disclose a wide range of oxysterol derivatives and synthetic LXR agonists (see pages 9-10 of the response). Applicant further assert the current pending claims are fully enabled by the specification and do not require undue experimentation based on the reasoning to the factors presented *in In re Wands* (pages 9-12 of the response). The response has been fully considered, however, the argument is not found persuasive because the specification only describe using a specific LXR agonist (compound 1, a sulfonamide) to treat diabetes, it does not disclose the treating conditions such as the dose for other LXR agonists containing different structures (e.g., oxysterol derivatives and TOFA as indicated in the references provided by applicants) in the treatment of diabetes, nor indicates the effects of these various LXR agonists in treating diabetes. Furthermore, the specification does not teach how to reduce the risk of developing or the risk of recurrence of diabetes using an LXR agonist. Moreover, the claimed method encompasses the use of unspecified LXR agonists, where the structures and the effects of the LXR agonists are not described in the specification, thus, as indicated in the section above, it requires undue experimentation to enable the full scope of the claims.

Conclusion

8. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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December 31, 2003

ROBERT A. WAX
PRIMARY EXAMINER